Imaging in metabolic research: challenges and opportunities

J Appl Physiol 124: 160–161, 2018;
First published October 12, 2017; doi:10.1152/japplphysiol.00906.2017.

EDITORIAL | *Imaging in Metabolic Research*

Imaging in metabolic research: challenges and opportunities

Vera B. Schrauwen-Hinderling[1] and Annemie M.W.J. Schols[2]

[1]*Department of Radiology, NUTRIM School of Nutrition and Translational Research in Metabolism, Maastricht University Medical Center, The Netherlands; and* [2]*Department of Respiratory Medicine, NUTRIM School of Nutrition and Translational Research in Metabolism, Maastricht University Medical Center, The Netherlands*

Submitted 3 October 2017; accepted in final form 4 October 2017

Metabolic alterations are involved in the etiology and progression of high burden chronic noncommunicable diseases including Type II diabetes, chronic obstructive pulmonary disease (COPD), and cardiovascular disease. Not only disease specific but also generic metabolic aberrations have been identified, which is not surprising because many chronic diseases share common lifestyle-induced risk factors, including smoking, physical inactivity, and dietary quality. Incorporating metabolic imaging in deep phenotyping may be an important step toward personalized medicine. Furthermore, metabolic imaging is an attractive noninvasive tool for integrative physiology, because it may provide information about crosstalk of various processes between different tissues, including, for example, inflammation, hypoxia, perfusion, substrate metabolism, and mitochondrial function. This Highlighted Topic series provides an overview of recent developments in metabolic imaging applications and methodological challenges in the context of physiological and clinical research questions. Scientists from different centers and departments were invited to discuss and share their views in joint reviews.

Although animal models have provided us with very valuable mechanistic insights in metabolic control, human validation can be challenging, and, therefore, the human relevance often remains unclear. This is at least in part due to the fact that in conventional research, tissue sampling is needed to get mechanistic information. While for the investigation of muscle or subcutaneous adipose tissue metabolism it is feasible and relatively easy to obtain tissue biopsies, such invasive procedures are generally not performed in other vital organs, and, therefore, noninvasive techniques are needed to gain information of the liver, the heart, the lung, the brain, or whole body metabolism. The application of imaging will advance our understanding of tissues that are not accessible for biopsies and will further deepen our understanding of the orchestration of metabolism on a whole body level and on organ crosstalk. An important feature of imaging techniques is that in many cases, dynamic measurements can be performed and therefore processes can be followed in time and the response to physiological challenges can be monitored.

Medical imaging methods are usually used for diagnostic purposes to determine presence or severity of disease in a clinical setting and to monitor treatment. However, their potential is much greater, and these techniques can also give valuable metabolic information that will help us understand normal physiology as well as abnormal metabolic control induced by disease or in the etiology of disease at a molecular level.

In this Highlighted Topic, various aspects of metabolic research are considered and the application of metabolic imaging methods in a range of topics is discussed. To this end, a set of invited reviews discusses the applicability of imaging techniques in studying cardiac, hepatic, and (brown and white) adipose tissue metabolism. Normal physiology is addressed in two reviews on exercise physiology and postprandial metabolism, respectively, and the application of imaging to investigate chronic disease complexity is addressed in a review focused on COPD as clinical model. These are now briefly described.

The review by Lundbom (2) on adipose tissue and liver elaborates on the use of dual-energy X-ray absorptiometry (DEXA), computed tomography (CT), and magnetic resonance imaging (MRI) for quantification of various adipose tissue depots and also discusses the possibility to characterize these depots in terms of fatty acid composition with ^{1}H-MRS. In the liver, ^{1}H-MRS has provided a lot of information during the last decade about so-called ectopic fat storage and ^{31}P-MRS has provided information on energy metabolism, which is also reviewed.

Van de Weijer et al. (6) nicely describe in their review on cardiac metabolic imaging, how magnetic resonance spectroscopy (MRS), MRI, positron emission tomography (PET), and single photon emission computed tomography (SPECT) can give complementary information in the study of fatty acid and glucose metabolism, mitochondrial function, and cardiac perfusion. They also summarize how the various PET and SPECT tracers that are available for human research can yield differential metabolic information.

The review by Chechi et al. (1) on brown adipose tissue (BAT) summarizes the recent advances in our understanding of brown adipose tissue metabolism and its relevance for whole body energy metabolism. BAT was rediscovered by performing PET scans with the glucose tracer fluorodeoxyglucose (FDG) after cold exposure and quantifying the subclavicular glucose uptake. In this review, the limitations of this method are discussed and potential methodological issues that should be taken into account in future studies.

The review on exercise physiology by Rudroff et al. (3) points out which methods can provide better understanding of the metabolic processes during exercise by either performing measurements before and immediately after an exercise session or by following the metabolic changes real time during exercise. It is described how PET measurements can be used to

Address for reprint requests and other correspondence: V.B. Schrauwen-Hinderling, Maastricht University Medical Center, Maastricht, Netherlands (e-mail: v.schrauwen@maastrichtuniversity.nl).

 8750-7587/18

determine changes in muscle metabolic activity and blood flow, and an application of SPECT is highlighted to investigate exercise effects on brain metabolism. Also the use of MRS in investigating muscle metabolism and the potential of near-infrared spectroscopy to investigate kinetics of tissue oxygenation is discussed.

The review of postprandial metabolism by Carpentier et al. (5) exemplifies the importance of dynamic information when biological processes such as the handling of a meal is discussed. The complimentary nature of MRS and PET (or SPECT) measurements can be appreciated, and a summary of the recent advances of our understanding of postprandial metabolism is given. The review by Sanders et al. (4) shows that the use of new analytical techniques applied to traditional imaging modalities (CT, DEXA) and the application of more novel imaging techniques (PET, hybrid PET/CT) have greatly improved understanding the complexity of COPD both at the level of the pulmonary system as well as regarding extrapulmonary manifestations.

This series of reviews provides a comprehensive overview of the huge potential for metabolic imaging in physiological research. Each imaging technique has advantages and disadvantages that need to be considered when designing a study. Importantly, the various techniques provide complementary information. While PET and SPECT are techniques that expose volunteers to radioactivity, they have the advantage that the use of tracers with varying characteristics can target a specific metabolic process (e.g., uptake vs. metabolism of a metabolite). Methods like MRS or near-infrared spectroscopy (NIRS), on the other hand, generally rely on the quantification of endogenous metabolites, do not expose volunteers to radioactivity, and can be repeated many times.

The noninvasive nature and the dynamic information that can be gained from the methods that are discussed are crucial in investigating metabolic changes that occur either in response to normal physiological challenges such as physical activity or a meal, but also to study the relevance of metabolic processes in chronic disease etiology and progression. Current methodological developments will certainly advance our possibilities for metabolic imaging in the future and novel MR sequences, higher sensitivity, and novel PET tracers will contribute to a much more detailed knowledge of human metabolism.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS

V.B.S.-H. and A.M.S. drafted manuscript; V.B.S.-H. and A.M.S. edited and revised manuscript; V.B.S.-H. and A.M.S. approved final version of manuscript.

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